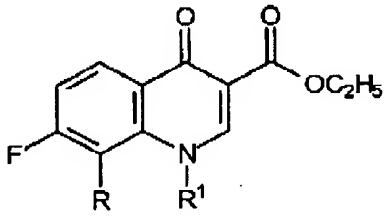
Appl. No. 10/630,608
Atty. Docket No. 9009
Amdt. dated April 26, 2004
Reply to Office Action of April 7, 2004
Customer No. 27752

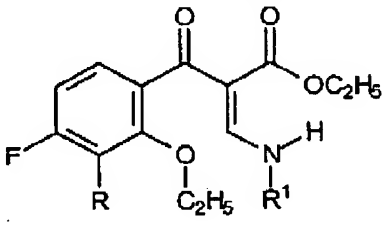
AMENDMENTS TO THE CLIAMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Original) A process for preparing a quinolone antibiotic intermediate having the formula:



wherein R is C_1-C_2 alkyl, C_1-C_2 fluoroalkyl, C_2-C_4 alkenyl, methoxy, chloro, or bromo; R^1 is a unit selected from the group consisting of C_1-C_2 alkyl, C_2-C_3 alkenyl, C_3-C_5 cycloalkyl, and phenyl, each of which can be substituted by one or more fluorine atoms; said process comprising the step of cyclizing an admixture of quinolone precursors, said admixture comprising a 2-ethoxy substituted intermediate having the formula:



in the presence of a silylating agent.

2. (Original) A process according to Claim 1 wherein R is $-OCH_3$.

3. (Original) A process according to Claim 1 wherein R is $-CH_3$, $-CH_2F$, $-CHF_2$, and $-CF_3$.

4. (Original) A process according to Claim 1 wherein R is –Cl.

5. (Original) A process according to Claim 1 wherein R is $-CH_2CH=CH_2$.

6. (Original) A process according to Claim 1 wherein said cyclization is conducted in the presence of a solvent selected from the group consisting of methylene chloride,

dichloromethane, hexamethylphosphoramide, tetrahydrofuran, benzene, toluene, alkanes, and mixtures thereof.

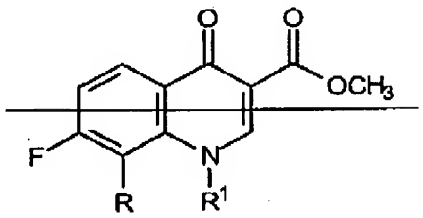
7. (Original) A process according to Claim 1 wherein said silylating agent is selected from the group consisting of chlorotrimethylsilane, N,O-bis(trimethyl-silyl)acetamide, N,O-bis(trimethylsilyl)trifluoroacetamide, bis(trimethylsilyl)urea, hexamethyltrisilazane, N-methyl-N-trimethylsilyltrifluoroacetamide, 1-trimethylsilyl-imidazole, trimethylsilyl trifluourmethanesulfonate, *tert*-butyldimethylchlorosilane, 1-(*tert*-butyldimethylsilyl)imidazole, N-*tert*-butyldimethyl-N-methyltrifluoroacetamide, *tert*-butyldimethylsilyltrifluoromethanesulfonate, *tert*-butylphenylchorosilane, *tert*-butyl-methoxyphenylbromosilane, dimethylphenylchlorosilane, triethylchlorosilane, trimethyl-silyl trifluoromethanesulfonate, and triphenylchlorosilane.

8. (Currently Amended) A process according to Claim 7 wherein said silylating agent ~~agents~~ is N,O-bis(trimethylsilyl)acetamide.

9. (Original) A process according to Claim 1 wherein R^1 cyclopropyl, methyl, ethyl, and benzyl. 4

10. (Original) A process according to Claim 1 wherein said cyclization is conducted by refluxing in the presence of a solvent.

11. (currently Amended) A process for preparing a quinolone antibiotic intermediate having the formula:



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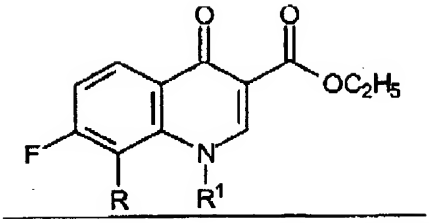
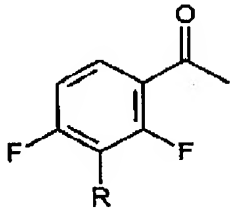
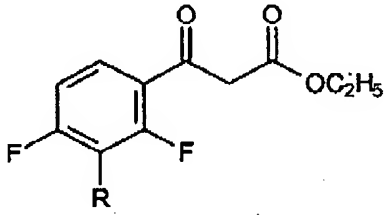


wherein R is C_1-C_2 alkyl, C_1-C_2 fluoroalkyl, C_2-C_4 alkenyl, methoxy, chloro, or bromo; R^1 is a unit selected from the group consisting of C_1-C_2 alkyl, C_2-C_3 alkenyl, C_3-C_5 cycloalkyl, and phenyl, each of which can be substituted by one or more fluorine atoms; said process comprising the steps of:

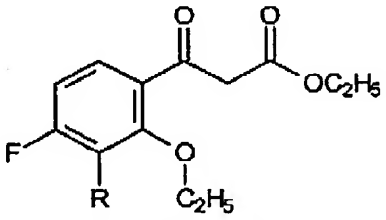
a) reacting an acetophenone having the formula:



with diethylcarbonate in the presence of a base to form an admixture of 4-fluoro β-ketoesters having the formula:

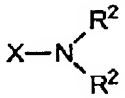


; and

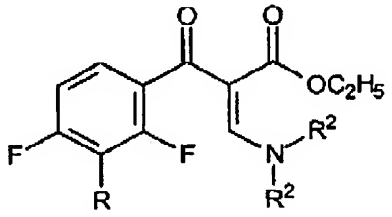


;

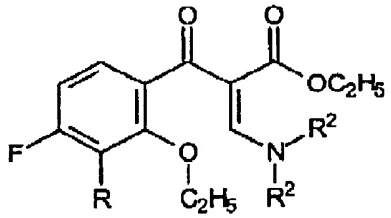
b) reacting said admixture with a Knoevenagel Reaction adduct having the formula:



wherein R^2 is C_1-C_4 linear or branched alkyl, phenyl, and mixtures thereof; X is an aldehyde unit or an aldehyde unit equivalent; to form an admixture of imine intermediates having the formula:



; and

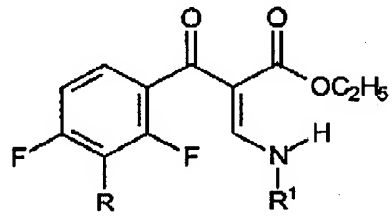


;

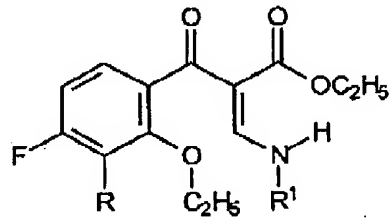
c) reacting said imine intermediate admixture with an amine having the formula: 6

$$R^1—NH_2$$

to form an admixture of quinolone intermediates having the formula:

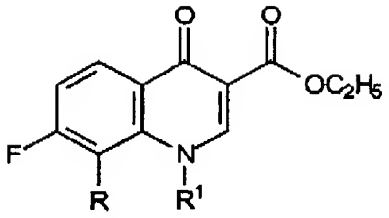


; and



;

d) cyclizing said quinoline intermediate admixture in the presence of a silylating agents ~~agent~~ to form said quinoline antibiotic intermediate having the formula:



12. (Original) A process according to Claim 11 wherein said base in step (a) is a metal hydride selected from the group LiH, NaH, KH, CaH_2 and mixtures thereof.

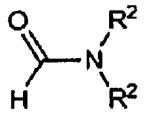
13. (Original) A process according to Claim 11 wherein said base in step (a) is an inorganic base selected from the group Na_2CO_3, $NaHCO_3$, K_2CO and mixtures thereof.

14. (Original) A process according to Claim 11 wherein said base in step (a) an organic base selected from butyl lithium and lithium diisopropylamide.

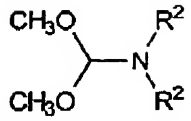
15. (Original) A process according to Claim 11 wherein step (a) comprises reacting one mole of a substituted acetophenone with 2.2 moles of a base, and 2.4 moles of diethylcarbonate.

16. (Original) A process according to Claim 11 wherein step (a) is conducted in the presence of a solvent selected from the group consisting of methylene chloride, dichloro-methane, hexamethylphosphoramide, tetrahydrofuran, benzene, toluene, alkanes, and mixtures thereof.

17. (Original) A process according to Claim 11 wherein said adduct is an aldehyde having the formula:



18. (Original) A process according to Claim 11 wherein said adduct is a dimethyl acetal having the formula:



wherein R^2 is methyl, ethyl, and mixtures thereof.

19. (Currently Amended) A process according to Claim 11 wherein step (b) is conducted in the presence of toluene wherein said adduct is a dimethyl acetal and wherein further the admixture obtained from step (a) and said dimethyl acetal is heated ~~heat~~ to azeotropically remove any methanol which is formed.

20. (Original) A process according to Claim 11 wherein said primary amine in step (c) is selected from the group consisting of methylamine, ethylamine, and cyclopropylamine.

21. (Original) A process according to Claim 11 wherein step (c) is conducted in the presence of a solvent selected from the group consisting of methylene chloride, dichloro-methane, hexamethylphosphoramide, tetrahydrofuran, benzene, toluene, alkanes, and mixtures thereof.

22. (Original) A process according to Claim 11 wherein step (d) is conducted in the presence of a solvent selected from the group consisting of methylene chloride, dichloromethane, hexamethylphosphoramide, tetrahydrofuran, benzene, toluene, alkanes, and mixtures thereof.

23. (Original) A process according to Claim 11 wherein said silylating agent is selected from the group consisting of chlorotrimethylsilane, N,O-bis(trimethyl-silyl)acetamide, N,O-bis(trimethylsilyl)trifluoroacetamide, bis(trimethylsilyl)urea, hexamethyltrisilazane, N-methyl-N-trimethylsilyltrifluoroacetamide, 1-trimethylsilyl-imidazole, trimethylsilyl trifluourmethanesulfonate, *tert*-butyldimethylchlorosilane, 1-(*tert*-butyldimethylsilyl)-imidazole, N-*tert*-butyldimethyl-N-methyltrifluoroacetamide, *tert*-butyldimethylsilyl-trifluoromethane sulfonate, *tert*-butylphenylchorosilane, *tert*-butyl-methoxyphenyl-bromosilane, dimethylphenylchlorosilane, triethylchlorosilane, trimethyl-silyl trifluoro-methanesulfonate, and triphenylchlorosilane.

24. (Original) A process according to Claim 23 wherein said silylating agents is N,O-bis(trimethylsilyl)acetamide.

25. (Original) A process according to Claim 11 wherein step (d) is conducted by refluxing in the presence of a solvent.